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FINAL REPORT

1965

# On the Transfer Function of Human Skin

by

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To the

U. S. Army Chemical Warfare Laboratory

Army Chemical Center

Maryland

Contract DA 18-109-405-CML-666

## Introduction

This report tries to clarify different aspects of transfer through human skin.

Water and water vapor are believed to move through intact skin surface by: a) glandular secretion such as that of sweat glands, b) sorption and desorption in the horny layer, c) diffusion through the horny layer. With proper care all three avenues can be sufficiently well differentiated. Sweating can be partly controlled by low room temperature, atropine and selection of a body area not prone to sweating. Sweat amount is also measured in blank tests on the opposite limb, furthermore by counting sweat droplets. Horny layer sorption and desorption is a saturation process after the skin enters a new environment. After sweat and sorption are evaluated or prevented, there remains a flow of liquid water or vapor through the skin. This flow seems to depend on the water concentration of the medium touching the skin. This concentration will be defined for water solutions, as well as for air, as relative humidity $r_a$. In all but a very few test persons water and water vapor, from solutions or air, of more than $r_a$ = 90 per cent, pass into the skin. Since the point of no transfer of 90 per cent relative humidity or about four osmolarity, the transfer should be active.

The active process or pump seems to be separated from the environment by a barrier. This barrier appears to be part or the whole of the stratum corneum conjunctum. Barrier and pump seem to be different entities with the following characteristics: a) the barrier: its resistance is about ten times higher on arm or leg than on palm or sole: about 3-5 times

higher for the same skin area under dry than under moist conditions: invariant to four hours of ethyl ether exposure: absent for about three days after stripping off the stratum conjunctum. b) The pump: its intensity is increased, (i.e., the neutral relative humidity is lowered) in persons having edema from toxemia, pregnancy, internal disorders and menstruation; the pump comes back to normal in about six days.

The first part of this paper concerns questions of skin water exchange by sweating, the second, those of diffusional water transfer in vivo, and the third, those of the barrier layer.

## I. Water transfer in vivo by sweating

### A. Hidromeiosis (with J. Hildebrandt)

The author's (1-3) skin water studies started with the discussion of papers by Robinson (4), Winslow (5), Weiner (10), Buettner (6) and others indicating an influence of skin moisture on sweat water loss. Since experiments were available with equal temperatures of skin and core, the difference obviously had to do with the presence of a water layer on the skin under moist conditions. This difference then could be explained by either a water backflow from the sweat covered skin or by an influence of this water on the sweat mechanism itself. The first process is open to experimental verification. Results of this verification are ample now (1, 2, 6, 7, 8). However, the backflow as observed on arm, foot, hand, and properly extrapolated for the whole body cannot exceed 20 gm $hr^{-1}$ for an adult whereas differences of people sweating in dry versus moist environment at the same skin temperature exceed 300 gm $hr^{-1}$ (see (6)).

It is unlikely that the observed backflow could increase that much in spite of the observation that more water flows into a foot which is active and warm and, therefore, more sweating as compared to cool and less sweating conditions (2).

This syndrome now might be connected with the often claimed sweat gland fatigue (12). Whether this descriptive term is a correct explanation of an observed fact seems doubtful now since Belding and Hertig (9, 11) demonstrated a strong decline of sweat water loss after about one hour if the person was in a warm tap water bath. Water of low salinity reduced sweating less and in a 10-15% NaCl bath sweating continued at a high rate for hours.

It seems, therefore, irrelevant whether sweat water or bathtub water covers the sweating skin.

In our own tests we first verified Hertig's basic statements by essentially repeating his experiments. In our tests sweating was produced on a person at rest in a hot bath; Hertig used, in addition, exercise to promote sweating. We then tried to contribute to the question: Is this phenomenon hidromeiosis centrally or locally controlled?

A constant temperature bath for total immersion of human subjects was built in collaboration with Sam Antion, technician of the Department of Meteorology. A thermistor-controlled on-off relay energizing a 1200 w heater regulates bath temperature to $\pm$ 0.05°C.

Initial experiments verified the decline in perspiration phenomenon or hidromeiosis reported by Hertig and Belding (9, 11). Additional vapor transfer measurements by the method of Buettner showed only slight, if any

increases in skin permeability after three hours in hot baths (36.7-37.3°C), negating the possibility of large scale reabsorption.

It was proposed to test directly the hypothesis proposed by Hertig, i.e., that the temperature receptors were being diluted by small amounts of water entering subcutaneous regions and thus lowering their firing rate (Diamond (12)). A consequence of such a mechanism would be a reduced drive from the central nervous system to all sweat glands, and small areas of skin kept dry should exhibit the same hidromeiosis as the rest of the body submerged in water.

Dry air was passed through a water-tight capsule strapped to the inner forearm, and the moisture collected in Drierite or $CaCl_2$ filled tubes. Flow rates were adjusted to 500 ml/min to ensure virtually complete dryness of the 12 $cm^2$ area of skin. Drying tubes were changed hourly and weighed. Three runs on the same subject (J.H.) all showed a constant rate of local sweating even though the whole body water loss recorded by hourly measurements, sharply declined after one hour.

These preliminary results suggest that the site of origin of the process giving rise to hidromeiosis is at the sweat gland itself, not at the receptor, or centrally. Possible mechanisms include: (1) lower rate of secretion by the gland as a result of impaired neuroglandular transmission, or as a result of reduced secretory capabilities of the glandular cells, both presumably as a consequence of inward diffusion of water; (2) increased reabsorption in the duct leading to the skin surface (normally less than 1%, Lloyd (13)); (3) obstruction of the duct as a result of progressive swelling, a possibility discussed by Hertig (thesis, 1960), and rejected

on the ground that the miliaria crystallina were never observed. This experimenter, however, experienced extensive itching for a period of two days following a trial, suggesting symptoms of the sweat retention syndrome (Rothman (14)).

A number of attempts were made to devise a method of continuously recording sweat rate from the capsule. The "Hygropak" (Hygrodynamics Inc., Silver Spring, Maryland) proved to be rapidly responding, but its nonlinearity, hysteresis, and drift precluded its use for the present application where absolute humidity (not relative humidty) over a fairly wide range is desired.

B. Anhidrosis (with A. Motulsky et al.)

Hereditary absence of functioning sweat glands is a rare disease which, however, for this project is of some interest because the disease may tell us something about the principle of sweating and also because the frequency of the disease will probably increase after air conditioning makes survival of afflicted people more likely.

The following joint report was given by our group:

"Anhidrotic Ectodermal Dysplasia"

A. Motulsky, H. Nyegaard, A. Schultz, Jean Crichlow and K. Buettner, Division of Medical Genetics and Dept. of Meteorology, University of Washington, Seattle, Washington

Anhidrotic ectodermal dysplasia is a genetic train causing anhidrosis, hypotrichosis and hypodontia. Eight patients in six kindreds were studied and the literature reviewed. The data confirm sexlinked inheritance. Of special interest was the occurrence of unilateral sweating, unilateral hypotrichosis and unilateral mammary hypoplasia in a female heterozygote

with the condition. This and other female heterozygotes were investigated with the starch iodine technique for sweating distribution. The occurrence of patchy sweating confirmed a similar report in the literature. This finding is compatible with the concept that female heterozygotes for ectodermal dysplasia are mosaics for X chromosomal function so that some cells function under control of the normal X chromosome while others function under influence of the mutant X chromosome.

Linkage investigations with colorblindness and the new sexlinked blood group $XG^a$ (in cooperation with Dr. Race and Sanger) are in progress. Crossovers between the locus of colorblindness and the $XG^a$ bloodgroup have already been found.

In the case we studied, the female was a hemihidrotic heterozygote. She sweated more on the left than on the right side of her body.

The afflicted males express the disease fully. There is no sweating, no eyelashes, or brows, poor teeth, and heavy frontal bones.

Five normal people were tested in a room where the temperature was 40-45°C. Sweating was measured with Minor's technique (starch-iodine). These measurements were compared to those of a family where the mother and one daughter were heterozygote carriers, one son expressed the trait fully and another daughter seemed to be normal.

Six normals were tested first, then the afflicted family. All controls and subjects were placed in a hot room (40-45°C). They were dressed in hospital bikinis, and were painted with Minor's iodine solution before entering the hot room. The dry starch was then applied with a puff. In certain areas, the starch and iodine were removed and the cedar oil technique (Jurgenson, 1924) was used: some vaseline was added to the cedar oil in order to raise its viscosity.

The demarcation of the left to the right side was quite marked for strongly sweating areas such as forehead, breast, and abdomen, much less for less sweating areas such as the leg. The ratio of sweat count of

normal to inflicted side was for forehead 10:1, breast 7:1, arm 4:1, waist 3:1, knee 1:1, leg 1:1. The girl lost in a 45°C dry room 160 gms.

## II. Transepidermal water diffusion

Folk and Peary (7) showed first a water inflow into the water covered human feet. Buettner (1-3) extended the tests to other skin areas and found this inflow to be general for normal skin and that of palms and soles. Behavior of such special skin areas as the inguinal, of strongly hairy areas, of the surrounding of body openings and of the area between the toes is not yet known.

During the time of this contract, methods and results of (1-3) were expanded. The new methods include a) Liquid transfer from small wetted gauze pads into or out of the skin of arm or foot sole. b) Prewashing with ether and addition of soap to method a). c) Application of more refined methods to prevent leakage, or to care for sorption in the horny layer which could be mistaken for true transfer. d) Longer vapor test applications in order to minimize errors mentioned under c).

All tests including the ones done with additional precautions confirm that a) water moves into the skin of arm and foot if its osmolarity is less than four. More concentrated solutions cause water outflow. b) Water vapor moves into the skin of arm and sole if the relative humidity of the air adjacent to the skin exceeds 90-95%. Skin and air temperatures are made equal. c) Details about the flow into the foot were especially investigated (with Tom Adams).

Water covering a human foot moves into it at a rate of 1/2 - 2 gm $hr^{-1}$ (1).

More factual data on this water inflow are listed below. The method has been slightly amended as time went by, but no essential changes were necessary. The present procedure is as follows.

One foot, the "wet" foot, is dressed in a layer of cotton cloth, a bag of polyethylene soft plastic, a plastic boot, all held tight around ankle and lower leg by elastic bandages. Before bandaging 60 gms of water are inserted at the foot. Finally a heavy leather boot is added as protection. The opposite or "dry" foot is dressed equally except for the omission of water. Additional plastic bags serve to receive all parts, except bandages and leather boot, after exposure. After the test the "wet" foot is dried with a weighed towel and both feet covered with dry cotton under a plastic cover for another 30 minutes. This is called the after blot test.

The observed loss of "wet" foot package is corrected for sweat transfer using the "dry" foot loss, also for corneal sorption of applied water from data of the first 30 minutes after blot test.

Times of exposure range from 5 hours to 30 hours.

Total number of tests from August 1960 to June 1962 is fifty.

Average intake of all tests is 1.42 gm $hr^{-1}$ per foot or 0.002 $cm^{-2}$ $hr^{-1}$ or 20 gm $m^{-2}$ $hr^{-1}$ which is smaller than the average value of 30 gm $m^{-2}$ $hr^{-1}$ reported earlier (1, see fig. 6) and equal the old value (1) for cool and/or at rest conditions.

Water went into the foot in all exposures including those using sea water or a 10% NaCl solution. Salt concentration has to exceed 15-20% to reverse this flow, as shown before (1).

(1).

It would be interesting to know where the water went after passing into

the foot. As shown before (1) the amounts surpass by far the sorptive capacity of the corneum. Also, if sorbed there, most of it would be regained in the after blot test. The water obviously moves deeper. To test its location, volume change measurements were added to the water transfer tests. The foot volume meter of Tom Adams consists of a water tight concrete boot, a system of communicating water containers including glass pumps and a communicating vertical open column. After the foot is inserted, water is added until it reaches a mark which is read by lense on the vertical column. Any changes of volume are equalized by adding or subtracting known amounts of water until the mark is reached again. "Wet" and "dry" foot are compared routinely.

During exposures both feet are equal with respect to exercise--if any--room conditions, etc. They only differ in being wet or dry. Any volume changes of the dry foot has, therefore, been used to correct volume changes of the wet foot. In this way forty volume changes have been measured.

Tentative results are as follows:

1. During daytime with normal laboratory work or while sitting the volume increases usually more than the water gain of the wet foot would indicate. We frequently see, e.g., a 3 $cm^3$ swelling caused by a 2 gm water inflow.

2. During the night the water gain went on at the same rate. The volume, however, decreased substantially. After a day and a night initial volume was reached again in some cases.

Swelling of hands from water absorption was reported earlier (1); it

can be quite painful on fingers. The fact that a "wet" foot swells by more than it takes in could indicate an edema caused by the foreign water. Exercise and hydrostatic pressure at daytime activity could enhance these conditions. The foot shrinking while in bed could mean a lessening of edematous conditions.

Of course, we do not know whether the swelling is caused by the foreign water or whether this causes an edema which actually contains body water or whether both factors work. However, the 24 hours test suggests that in the end all foreign water moves into the system.

## III. The role and location of the barrier

It was discovered about one year ago that the frequently used method of Szakall (19, 20) for separating the corneum conjunctum leads to gross errors. By separating the stripped layer from the adhesive tape using petroleum ether large amounts of the soluble fraction of the adhesive tape glue are obviously forced into the skin layer. This falsifies results as follows:

1) The water soluble fraction is about 40%; 4% is the correct value. Most of the solute in Szakalls test is tape glue.

2) The soluble fraction contains proteins or at least large molecules which belong to the tape glue.

3) The diffusion resistance to water and alcohol vapor is controlled by the tape glue.

4) The change of this resistance with relative humidity is also due to the tape glue.

5) The subsequent effect of petroleum ether, tape glue and water seem to permanently alter the layer.

All former tests made with solvents to remove the skin layer from the tape are wrong.

For our new tests the layer is removed mechanically from the adhesive tape; this has to be done immediately after skin stripping.

It is commonly accepted that skin wet from sweating or prolonged water application is clammy and very stretchable (14). Skin separated from the atmospheric environment for a long time by impermeable layers of oil, grease or plastics feels less clammy; the reason for this will become apparent later. Very dry skin feels brittle, can be stretched very little, and breaks easily.

Where are the barrier layers? In stripping the outer layers, stratum corneum disjunctum comes off easily in incoherent bits and pieces. It cannot be a barrier except for mechanical protection. It might be like callus in this sense, which has a water vapor resistivity more than one hundred times lower than that of the Szakall layer.

The next layer is the Szakall layer, previously called the stratum corneum conjunctum (scc), which also is easily stripped. This layer is defined solely for its easy strippability. Only part of the total resistance to water and alcohol is located here. The change of water vapor transmittance with relative humidity, a change which is so typical for horny substances (15), is not evident with the Szakall layer. Passage through this layer might therefore be in vapor form through submicroscopic holes. It is not known yet whether this layer is identical with Brody's

intermediate layer (16), which is composed of about three flattened cell layers. If this is the case, Brody's basal layer might possibly be identical with the lower barrier, tentatively called the Mali layer. The lower barrier contains (Table 1) the bulk of the diffusion resistance, and its water vapor resistance varies with relative humidity as it should for true horny substances.

It could also be argued that the Szakall layer is the only barrier, but that the stripping process damages it to such an extent that data in vivo are not comparable. For the original Szakall process, using petroleum ether to remove the adhesive tape glue, this certainly is the case. With the new mechanical technique of removing the Szakall layer there can be no chemical contamination except by the possible remnants of the tape adhesive on the layer. Such remnants have not been detected on any of the pieces used for transfer tests when examined with the polarization microscope. Also, no holes could be discovered. However, the question whether stripped-off Szakall layer is usable to represent living conditions has still to be answered.

King (15) demonstrated that the water vapor diffusion resistance of horn increases ten times when the relative humidity declines. The latter value is the average of the humidities on both sides of the piece of horn in the test chambers. This change of resistance is thought to be caused in part by the higher hygroscopicity or water uptake at high rather than at low relative humidities, and in part by an easier liquid water transfer through moist horn. Mali (17) discovered the same phenomenon with excised skin even after stripping with adhesive tape; in this particular case a

barrier layer without the Szakall layer is probably involved. Buettner (1, 2, 18) found a similar change of diffusion resistance with either relative humidity or with the osmolarity of the solution applied on the living skin of arm, hand, and foot. (Osmolarity = molarity x van't Hoff's dissociation constant.)

It is sometimes convenient to compare callus and lower horny layer. Callus is easily available in large quantities. It shows similarities to the horny layer in its mechanical change of behavior with relative humidity. Both consist mainly of keratin. However, they are quite different in two important aspects. First, the Szakall layer is much more hygroscopic than callus (Fig. 1). Secondly, callus and Szakall layers differ grossly in their water vapor diffusivity (Table 1). That of the Szakall layer compares well with that of rubber and plastics, that of callus is one hundred times higher than that of the barriers (Table 1).

Blank's tests were made at 23°C with humidities of 100% and 18%, respectively, on both sides of the test chamber (21). Blank and Mali's (17) diffusivities are calculated from their data. Thickness data for callus are those given by Blank; those for the barrier are estimates from electromicrographs and weighings. It is assumed that both the Szakall layer and the Mali layer are each 3μ thick, the latter estimate being very tentative.

As Blank (21) has shown, water is the only known compound which can change the mechanical properties of callus. Christopher and Kligman, as cited by Flesh (22) describe the remarkable behavior of strips of human horny layers. These layers can be easily stretched to twice their length

when moist, but they stretch only 10% when held below 65% relative humidity.

What Controls Skin Humidity

What is the relative humidity (rh) of the Szakall layer which as the first barrier, is exposed to extreme variations of rh? Buettner (23, 24) measured the rh and temperature of skin at many body areas directly. The rh was tested by bringing a hygrometer with one single hair in contact with the skin. In an unventilated room the data shown in Fig. 2 were found; here $\Delta p_w$ is the average water vapor pressure difference between skin and air. Below 30°C skin temperature sweating can be excluded. Obviously $\Delta p_w$ and convective air transfer control the vapor flow, also called insensible skin perspiration. This figure is notoriously independent of air humidity as long as sweating is absent, a fact which has been explained (2) by the increase of diffusion resistance at low humidities. The data of Fig. 2 may therefore hold for a wide range of conditions. It is then easy to calculate the average skin relative humidity $rh_s$.

$$P_{ws} = P_{wa} + \Delta p_w = rh_s \, P_{wssat} \qquad (1)$$

or

$$rh_s = (P_{wa} + \Delta P_w)/P_{wssat} \qquad (2)$$

where $P_{ws}$ and $P_{wssat}$ are the real and the saturation vapor pressures at the skin surface, and $P_{wa}$ is the air vapor pressure. For 35°C $P_{wssat}$ = 42 mm Hg. In a summer desert $P_{wa}$ is about 10 mm Hg. and in cold winters $P_{wa}$ may well be below 1 mm Hg. The ensuing values are $rh_s$ = 38% and 25%,

respectively.

With even slight ventilation, the $\Delta P_w$ figures nearly vanish, as tests show. The insensible perspiration is, however, about the same since the lower $\Delta P_w$ is compensated for by the higher convective transfer coefficient. In this case, with $\Delta P_w$ = 1 or less, critical $rh_s$ values are below 10%, at 35° skin temperature and at air values of $P_{wa}$ below 3 mm Hg. or a dew point of -6°C (21°F). These are precisely the conditions under which chapping begins, according to Gaul and Underwood's (25) observations in the winters of Indiana. Chapping is severe below -13°C (8°F) where $P_{wa}$ is 1.6 mm Hg., and the skin surfaces may suffer when $rh_s$ is below about 5%. Correlation of chapping and barometric pressure is coincidental; the weather controls $P_{wa}$ and air pressure. Fig. 3 shows these skin humidities graphically.

The barrier layers exhibit a large humidity gradient in dry air. In the extremes mentioned above, relative humidity changes from probably 90% just below the barriers, to near 5% at the surface (or a change in water vapor pressure from 38 - 2 mm Hg. over a depth of maybe 6μ). The barriers could break in the chapping process by (a) an especially low humidity in one sensitive sublayer, (b) an over-all low humidity, (c) a too high humidity gradient in the barriers or (d) a combination of these factors. It should be mentioned that there is practically no temperature gradient in the layers.

In working with hair hygrometers, one soon learns about their erratic behavior at low humidities. Hair changes its length most strongly at low humidities. Also near zero humidity it shows maximum shrinkage or shortest

length. This shrinking process is often interrupted by a spontaneous sudden lengthening, obviously caused by the breakage of some sublayers. This spontaneous lengthening occurs even when the applied tension is rather small. Both the shrinking and the spontaneous lengthening of hair might be expected to occur in corneum as well. The shrinking might itself cause an increase of tension and subsequent breaking. On the other side, different sublayers of the corneum might shrink differently in this steep humidity gradient.

The Relative Humidity of the Barrier Layer

If pliability, chapping, emollience and other mechanical factors of the upper skin depend on its water content, and if (Fig. 1) this content depends on the relative humidity, a study of its magnitude is important. Two conditions must be considered. If a large amount of air or relative humidity, $rh_x$, blows over an exicsed piece of horny layer, that layer will assume the same $rh_x$ in due time. If large amounts of this excised skin layer contact a limited amount of air of any initial rh value, the air will in due time show the value $rh_x$. The product $rh \cdot p_w$ sat = $p_{ws}$.

Since temperature differences in the upper layers are minute, $p_{wsat}$ is usually the same for all layers concerned.

Any vapor transfer is controlled by the difference of $p_w$ on two sides of a barrier layer and the diffusion resistance R of the layer. If we assume a series of barrier layers on top of each other called 01, 12, 23, etc., where 0, 1, 2 designate the border areas between the layers, then in equilibrium the vapor flow Q for three layers is found as:

$$Q = (p_{w0} - p_{w1})/R_{01} = (p_{w1} - p_{w2})/R_{12} = (p_{w2} - p_{w3})R_{23} = (p_{w0} - p_{w3})R \qquad (3)$$

where $R = R_{01} + R_{12} + R_{23}$.

If the temperature is constant, this may be written as

$$Q/p_{w\ sat} = (rh_0 - rh_1)/R_1, \text{ etc.}$$

The value $rh_3$ is the relative humidity at the surface and can be directly evaluated as shown above. Intermediate values $rh_1$ and $rh_2$ can be only found indirectly. $rh_0$ is the relative humidity in equilibrium with the living matter below the essentially dead barrier layers. As shown elsewhere (2), this value is not that of body isotonic fluids or $rh_0$ = 99.3%. It is much lower; namely $rh_0$ = 85 to 95%. This indicates that below the skin exists a pump or active transfer agent creating a 4 osmolar solution. Anatomy and function of this pump are still mysteries. The pump causes water and water vapor inflow into the skin of arm, hand and foot if the skin touches either water of less than 5% salt concentration or is surrounded by air at skin temperature of more than 90% relative humidity. This pump has also an important effect on skin pliability. It causes skin under grease or plastic cover to become moist (90%) but not stickily wet (100%), as mentioned above.

The outer relative humidity $rh_3$ depends, as described, on the environment on the inner conditions. Under calm conditions $p_{w3}$ can be (see above) up to 6 mm Hg. higher than the environmental air. With wind this difference nearly disappears.

The Barrier Layers

A barrier layer was first recognized by Blank (21) who stripped the corneum with adhesive tape. After the tenth stripping the vapor loss

multiplied, the barrier function vanished, or, in terms used here, R became small. The stripped-off layer later was isolated by Szakall (19) who separated it from the tape by petroleum ether. On the other hand, Mali (17) stripped excised skin and found no significant change of R. How can Blank's and Mali's statements be reconciled?

Stripping of living skin injures the layers below; the injured strata react with lymph and blood flow. If there is a barrier below the one stripped by Blank and Szakall it cannot be found in vivo by this technique. The layer so separated can be called a barrier, but not the barrier. In dead skin no reaction of the second barrier from stripping is expected. It is proposed to call the first barrier the Szakall layer and the second the Mali layer.

The following evidence is cited to show that there are at least two barrier layers located at the base of the horny layer:

(1) As mentioned before, Mali (17) stripped dead skin and found little difference in diffusion resistance.

(2) As shown elsewhere (1), the total diffusion resistance in vivo is about five times higher when skin is exposed to dry air than when exposed to air near 100%. This change is characteristic for keratin such as horn (15). This change cannot be observed in Szakall layer in vitro (Table 1) whereas it was falsified by the tape glue. It is truly evident, however, in Mali's tests in vitro (Table 1).

(3) The total diffusion resistance for water vapor in vivo at dry conditions is 5 - 10 times higher than that of Szakall layer in vitro also at dry conditions.

(4) The same is true of methanol and ethanol vapor transfer. Here the diffusion resistance is about ten times higher in living skin than in Szakall layer in vitro.

(5) Marzulli and Tregear (26) reported that stripping removed only part of the excised skin's resistance against radioactively labelled insecticides.

(6) Onken and Moyer (27) placed excised skin on a capsule with water on the inside and dry air outside. For 9°C and 40°C they found R = 5.4 and 4.8 $m^2$ hr mm Hg/gm, respectively. This value does not change much if the specimen is digested in 3% trypsin for 24 hours at 37°C. Stripping causes an uneven loss of stratum granulosum and a lowering of the diffusion resistance, not its disappearance.

(7) Brody (16) differentiates on electronmiscogram analysis an upper layer or stratum corneum disjunctum, an intermediate of there flattened cell layers which might be the Szakall layer, and a basal layer which might be the Mali layer.

A change of diffusion resistance with environmental humidity exists also in animal skin. Excised skin of rat has R = 0.7 and R = 0.2 $m^2$ hr mm Hg/gm for 50 and 90% relative humidity, respectively. Separated guinea pig epidermis shows much high diffusion resistance. We have R = 33 and R = 10 for 50 and 90% relative humidity, respectively. (These data are evaluated from the originals given by Edward J. Singer in personal communication.)

Together with Tom Ryan and Winston Jones, I could recently recheck some of the above statements.

Trypsin digested cadaver skin gives water diffusion resistances very much like those *in vivo*; the resistance also is higher in dry than in moist conditions.

Treating this layer with hexane and ether in a Soxhlet instrument removes the barrier quality. It should be recalled here that a four hour exposure to ether *in vivo* does not remove this barrier quality.

Contrary to Onken and Moyer (27) it is not possible to remake the barrier by adding the solute to it again. It is assumed that the true barrier lies in complicated lipoprotein bridges which cannot be replaced by any means.

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## TABLE 1

Water Vapor Diffusion Resistance R, Thickness dx and Water Vapor Diffusivity k of Different Materials

For explanation: The water vapor flow Q (gm $m^{-2}$ $hr^{-1}$) is $Q = (p_{w1} - p_{w2})/R$ where $p_{w1}$ and $p_{w2}$ are vapor pressures (mm hg) on both sides of the layer and R ($m^2$ hr mm Hg $gm^{-1}$) is the diffusion resistance. Thickness dx is given in μ where known, data in parenthesis are estimates. If dx is known, diffusivity k ($10^6$ $cm^2$ $sec^{-1}$) can be evaluated by $Q = k \frac{d\rho_w}{dx}$ where Q is now in units of gm $cm^{-2}$ $sec^{-1}$ and $\rho_w$ denotes vapor densities (gm $cm^{-3}$) on both sides of the layer.

King's (15) original k data are for concentration or density of liquid water, not water vapor in the piece of horn; data in this table are converted.

"Dry" means an average humidity of the layer near 50%, "moist" near 95% relative humidity.

| | | R | | dx(μ) | k | k |
|---|---|---|---|---|---|---|
| | | dry | moist | | dry | moist |
| 1. | Living Skin [Buettner (1, 2)] | 2.5 | 0.6 | (6) | 8 | 30 |
| 2. | Mali Layer [Mali (17)] | 4.1 | 1.6 | (3) | 2.3 | 6.5 |
| 3. | Callus [Blank (21)] | 0.7 | 0.19 | 200 | 1000 | - |
| 4. | Szakall Layer [Buettner] | 0.3 | 0.3 | 3 | 30 | 30 |
| 5. | Horn [King (15)] | | | 50 | 100 | 1400 |
| 6. | Paraffine [Blokker] | | | | 0.15 | - |
| | Ebonite [Blokker] | | | | 4.5 | - |
| | Soft Rubber [Blokker] | | | | 24 | - |
| | Cellophane [Blokker] | | | | 600 | - |
| | Air | | | | 280,000 | 280,000 |

Fig. 1

Relative weight increase of "regain" of different skin layers for varying relative humidities or room conditions. Abscissa is not linear but proportional to $(rh)^2$. In ordinate w = weight.

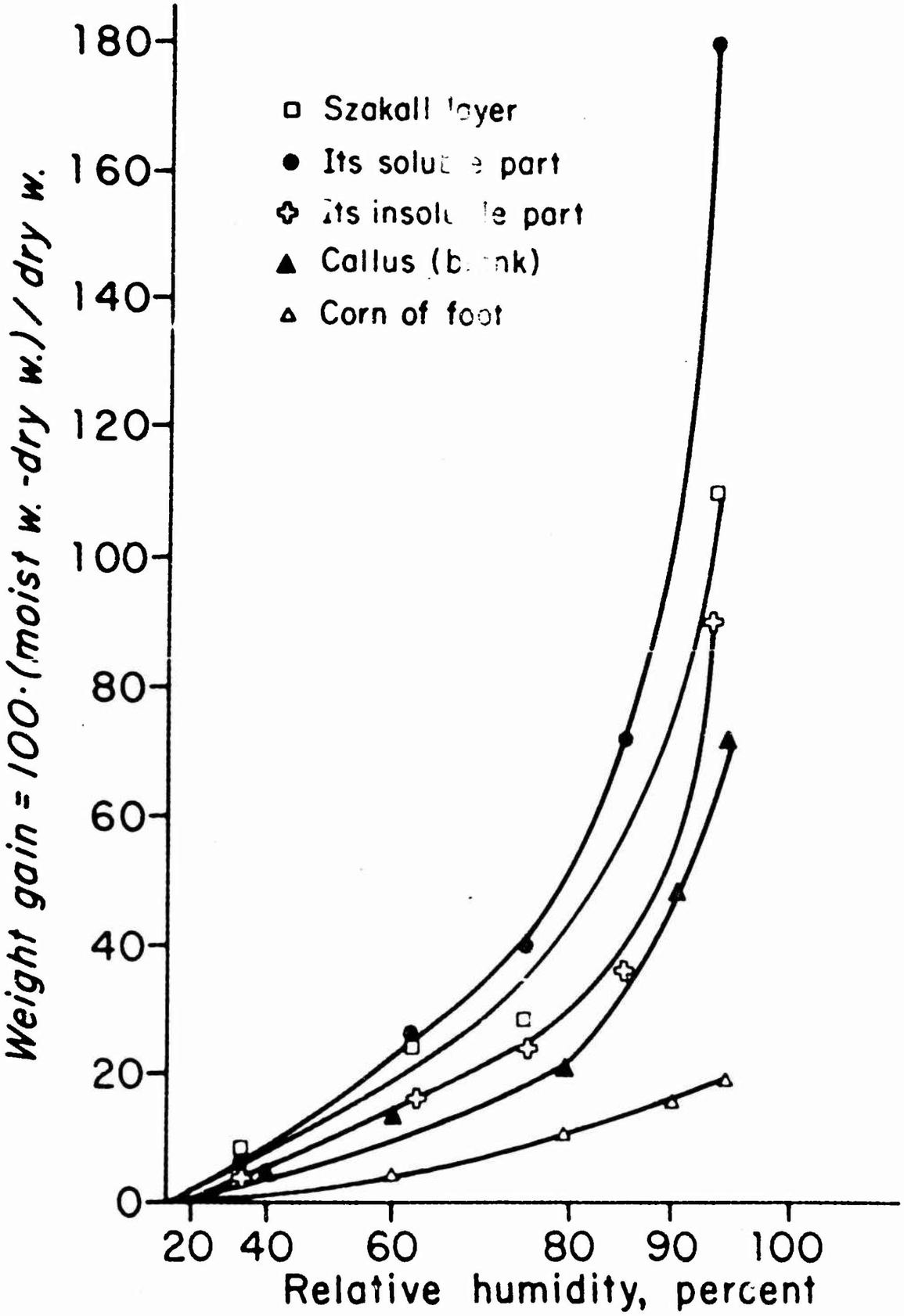
Fig. 2

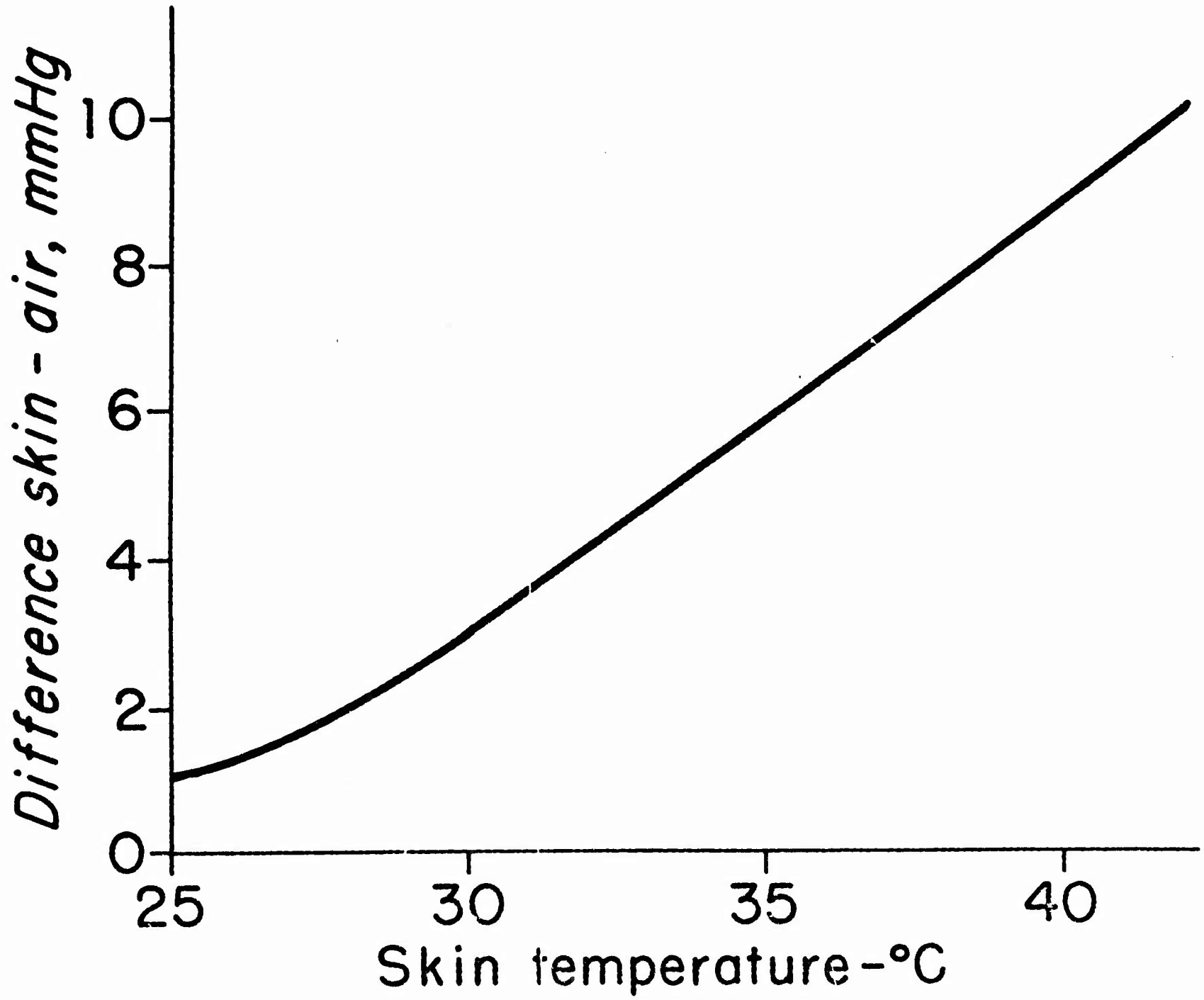
The difference between water vapor pressure at the skin surface and of air at some meters distance vs skin temperature. People at rest, average of forehead, chest, abdomen, thigh, shoulder, calf, backs of hand and foot. Room not ventilated. More than 50 test persons. Skin vapor pressure is measured using contact hair hygrometer and contact thermocouple. From (23).

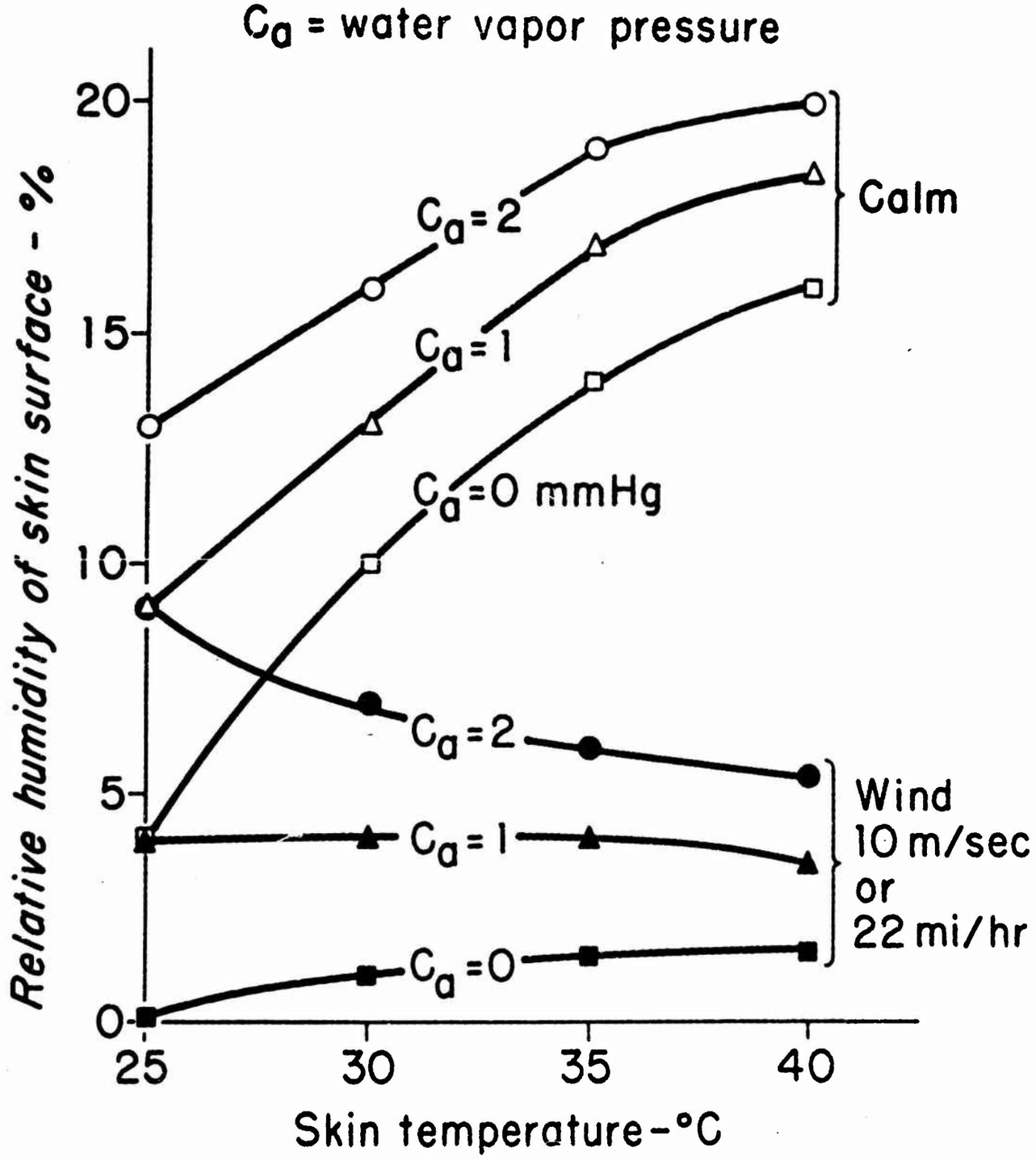
Fig. 3

Expected relative humidity of skin surface for given skin temperature (abscissa), given ventilation (two sets of curves) and given air vapor pressure Eq. (2) and Fig. 2 are used. Also (see (23)) the reduction of $\Delta p_w$ from ventilation.

($p_{wa}$ figures on lines.)


Szakall layer
Its soluble part
Its insoluble part
Callus (blank)
Corn of foot
Weight gain = 100·(moist w.-dry w.)/dry w.
180
160
140
120
100
80
60
40
20
0
20
40
60
80
90
100
Relative humidity, percent


Difference skin - air, mmHg
0
2
4
6
8
10
25
30
35
40
Skin temperature - °C


$C_a$ = water vapor pressure
Relative humidity of skin surface - %
20
15
10
5
0
25
30
35
40
Skin temperature - °C
$C_a$ = 2
$C_a$ = 1
$C_a$ = 0 mmHg
Calm
$C_a$ = 2
$C_a$ = 1
$C_a$ = 0
Wind
10 m/sec
or
22 mi/hr